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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,697	09/16/2003	Cheng Li		5503

7590 01/09/2008

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

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01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,697	LI ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,9-13 and 18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6, 9-13, 18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 19, 2007 has been entered.

2. The amendment filed, Oct. 19, 2007 is acknowledged. Claims 5, 18, 19, and 28 were amended and claims 7-8 and 14-17 were canceled. Claims 3-6, 9-13, 18-29 are pending in this application.

Election/Restrictions

3. Applicant's election with traverse of election of species in the reply filed on species NH2-GLY-THR-PRO-GLN-ILE-ALA-GLY-ARG-GLY-VAL-VAL)4-(Lys)2-Lys-β-Ala-COOH is acknowledged.

4. The indication of allowability of the species NH2-GLY-THR-PRO-GLN-ILE-ALA-GLY-ARG-GLY-VAL-VAL)4-(Lys)2-Lys-β-Ala-COOH is hereby withdrawn in light of the rejection cited below.

5. All rejections made in the previous office action and not cited herein are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 3-6, 9-13, 18-29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous office action and the reasons set forth below.

Applicants argue the claims have been limited where R variable in the MAP structure has been defined where it contains the peptide GTPGPQGIAGQRGVV in a polypeptide up 100 amino acids. Applicants make reference to paragraphs [0100] and [0107], tables 3-6 for support. Regarding Z variable, Applicants argue that the examples provide lysine, ornithine, or beta-alanine a variable Z. "With regard to working examples to support adequate written description, the poly amino acids, polylysine, and polyornithine, were well known in the art as of the filing date of the application." Thus, the specification provide ample written description.

Applicants arguments have been fully considered but have no been found persuasive.

First, regarding Applicants assertion that "the poly amino acids, polylysine, and polyornithine, were well known in the art as of the filing date of the application," Applicants have not provided any evidence to support this notion. Applicants have not made any reference to journal articles that would clearly establish "the poly amino acids, polylysine, and polyornithine, were well known in the art as of the filing date of the application" in the context of the claimed MAP structure. Mere knowledge of polylysines and polyornithines in the art does not serve to provide written description their use in MAP structures as claimed. Furthermore, the claims still allow for

up to 500 amino acids when the Z is polylysine or polyornithin. While polylysine may be recited in the specification, the specification is void of any specific guidance that the polylysine is indeed 500 amino acids in length. Applicants make reference to the web-site MP Biomedicals to illustrate that a polylysine homopolymer of 500 amino acids. However, the specification, as originally filed, does not make reference to this web-site and secondly the originally filed specification does not imply the use of polylysine homopolymers. In fact, when discussing polylsyines, the specification does not make reference to any homopolymers. Further, the specification does not provide a single working example where a polylysine homopolymer is used as the Z variable. Assuming arguendo that the specification does provide support for polylysine homopolymer, it is unclear how this provides written description for any peptide of up to 500 amino acids containing lysine, polylysine or ornithine. The claim state that Z contains lysine, polylysine, and ornithine, and is up to 500 amino acids. A reasonable interpretation of this definition includes sequences up to 500 amino acids that contain one or few lysine residues, along with other amino acids residues. The specification does not provide a single example of a Z variable with greater than a single lysine residue (see page 30-45).

With regard to the R variable, while the GTPGPQGIAGQRGVV, provides some insight into the structure, this sequence accounts for only fifteen of the 100 amino acids. As it has been stated in the previous office actions, The specification is void of any peptides that have a length of greater than 20-25 amino acids in length. There is no disclosure any peptides of sequences containing 100 or thousands of amino acids as the claims recite. The claims still allow for 85^{20} different possibilities of amino acids that constitute the R variable. Applicants make reference to to paragraphs [0100] and [0107], tables 3-6 for support for the claimed peptide. However, in reviewing these paragraphs, not a single example has been provided where the sequence

GTPGPQGIAGQRGVV resides in a much larger sequence. Thus, one cannot readily conclude that specification as filed provide ample written description of the claimed invention.

Rejection is maintained.

New Grounds For Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3-5, 9-13, 19-29 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 has been amended to recite "each R when present in the MAP structure comprise a total of up to about 100 amino acids, and where in R1 to R15 **is** GTPGPGIAGQRGVV." The amendment to the claims renders the claim indefinite because it the length of R1-R15 is unclear. While the claims states each R contains up to 100 amino acids, the claim also define R1 to R15 as GTPGPQGIAGQRGVV. It is unclear if the R variables are peptides of the sequence GTPGPQGIAGQRGVV having this exact length or are peptides containing GTPGPQGIAGQRGVV which can include N- and/or C- terminal amino acid additions up to 85 amino acids so the total amino acids are 100.

Claim 25 states that the MAPs are selected form MAP ID NO 13-MAP ID NO 48. However, many of these MAPS do not contain the required sequence GTPGPQGIAGQRGVV. Thus, the claim does not further limit the independent claims.

8. Claims 6. 9, 23 objected to under 37 CFR 1.75 as being a substantial duplicate of claims 4 and 22. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

New Matter

9. Claims 3-6, 9, 11-13, 20-24, 26-27, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite "Z is independently selected from the group consisting of lysine, polylysine, β-alanine, ornithine, or polyornithine," and "each Z when present in the MAP structure as polylysine or polyornithine comprises total of up to 500 amino acids." The addition of β-alanine, polyornithine and each Z as polyornthine up to 500 amnino acids constitutes new matter.

Lack of Literal Support

In reviewing the specification, Z was defined as "lysine, polylysine, ornithine, or any known trifunctional organic or inorganic linkers" (see page 11 and originally filed claims). The terms β-

alanine, polyornithine were never used to define the Z variables. In fact, the work polyornithine does not even appear in the originally filed specification. Thus, the specification cannot be said to provide literal support for β-alanine, polyornithine when defining the Z variable.

Lack of implicit/inherent support

" While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, **implicit, or inherent disclosure**." The instant specification also does not provide any implicit or inherent support for the amendments made to the claims. As stated earlier, the Z variable has been defined as lysine, polylysine, ornithine. Looking to the examples on pages 23-26 and table 3 on page 30-45, all of the Z variable are defined to be lysine. None utilize polyornithine or β-alanine. The specification only discloses the use of β-alanine for the X variable and not Z variable. Thus, reading the specification as a whole one cannot readily conclude that disclosure contains implicit or inherent support for the new amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and

invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3-6, 9-13, 18-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dang et al. (US2003/0113478) in view of Tam (Peptides: synethesis, structures, applications).

The claims are drawn to a peptide comprising a MAP structure conjugated to a substrate.

The reference of Dang et al. teach stents and grafts and means of coating them with a peptide. The reference specifically disclose coating a substrate with the sequence GTPGPQGIAGQRGVV (called P-15) have the ability to provide enhanced endothelial cell growth in vitro. The example characterized the P-15 surface treatment on ePTFE graft material, and measured its biological activity on the adhesion, migration and proliferation of endothelial cells in vitro. Also shown is the level of P-15 treatment degradation after simulated aging. The results show that this treatment method, characterized by the covalent attachment of a cell-adhesion peptide, was shown to be clean and stable. The surface treatment one PTFE grafts promoted the migration and proliferation of healthy endothelial cells. (see paragraph [0093]). The reference also states that the nature of the substrate to be coated may vary widely. At least a portion of at least one surface of the substrate 10 is coated with the functional group 16 or surface-modifying group 18 of the present invention. Preferably, the entire surface is coated with the functional group 16 or surface-modifying group 18. Suitable substrate materials include all non-porous or porous polymeric substrates, such as polyurethanes, polyamides, polyesters and polyethers, polyether-blockamides, polystyrene, polyvinyl chloride, polycarbonates, polyorganosiloxanes, polyolefins, polysulfones, polyisoprene, polychloroprene, polytetrafluorothylene (PTFE), polysiloxanes, fluorinated ethylene propylene, hexafluroropropylene, polyethylene, polypropylene, nylon, polyethyleneterephthalate, polyurethane,

silicone rubber, polysulfone, polyhydroxyacids, polyimide, polyamide, polyamino acids, regenerated cellulose, corresponding copolymers and blends, and also natural and synthetic rubbers. A substrate of particular interest to the present invention is expanded PTFE (ePTFE) (see pagargraph [0057]). Note that these meet the limitation of claim 4. The difference between the prior art and the instant application is that the reference does not disclose the MAP structure.

However, Tam teaches the synthesis and Application of branched peptides. The reference disclose the MAP structure where the Z variables are Lysine residues the dimeric (MAP2), tetrameric (MAP4), or octameric (MAP8) lysines are conjugated to a beta alanine residue (see page 458). The reference discloses that numerous peptides have been incorporated into MAP structures, differing in length and size (See table II). The reference disclose that MAP structure can be applied in immunoassays, seradioagnosis, epitope mapping, inhibitors, artificial proteins, and various biochemical studies and purification methods (see page 474). The reference states, as inhibitors, branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact (see page 476). Clustering could be achieved by adsorptoin on a surface or by coupling to a carrier or sepharose bead (see page 476). Observations of increased binding of branched peptides to cell surfaces, relative to the monomer, have been observed (see page 476).

It would have been obvious to one of ordinary skill in the art to incorporate the peptide GTPGPQGIAGPRGVV into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding of to cell surfaces, relative to the monomer. Note that the primary reference disclose that the peptide promoted the migration and proliferation of healthy endothelial cells. There would have been a reasonable expectation of

success because MAP branched peptides have been shown to have increased binding of to cell surfaces. Tam teaches that the Clustering, which allows for stronger binding than their monomers by allowing multiple points of contact could be achieved by adsorptoin on a surface or by coupling to a carrier or sepharose bead. Finally, Tam teaches numerous MAP structure and the means of making such structures.

11. Claims 3, 5, 10-13, 18-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar (WO9102537) in view of Tam (Peptides: synethesis, structures, applications).

The claims are drawn to a peptide comprising a MAP structure conjugated to a substrate.

The reference of Bhatnagar et al. teach the peptide GTPGPQGIAGQRGVV (called P-15) (see abstract). The reference discloses that the peptide is useful in promoting vertebrate cell adhesion to a substrate when the substrate is coated with the peptide (see page 4 of the reference). The reference also states that the peptide can be used to raise monoclonal antibodies against the epitopic region defined by P-15 (see page 10). Regarding the use for promoting vertebrate cell adhesion, the peptides are attached to a substrate such as glass, plastic, ceramics, organic polymers, gels, silica (see page 11). The reference disclose the means of covalently lining the peptide to the substrate (see page 11). The difference between the prior art and the instant application is that the reference does not disclose the MAP structure.

However, Tam teaches the synthesis and Application of branched peptides. The reference disclose the MAP structure where the Z variables are Lysine residues the dimeric (MAP2), tetrameric (MAP4), or octameric (MAP8) lysines are conjugated to a beta alanine residue (see page 458). The reference discloses that numerous peptides have been incorporated into MAP structures, differing in

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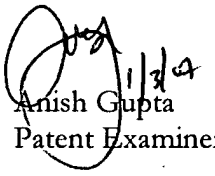
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach

the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.



Anish Gupta
Patent Examiner